

Fig. 1

# 3D structure topology

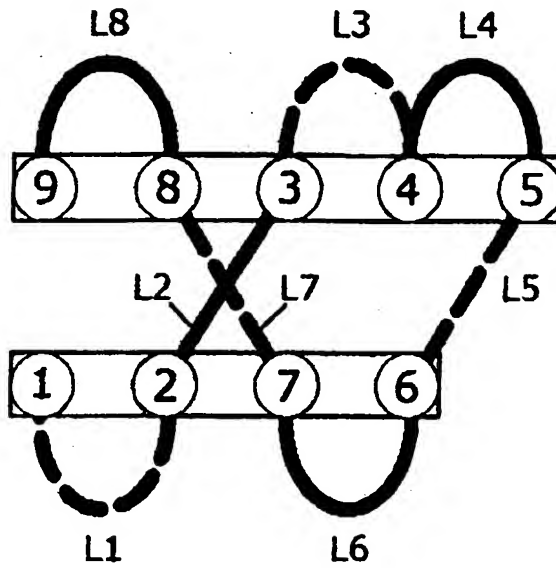
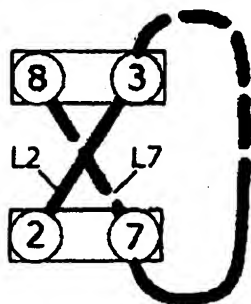


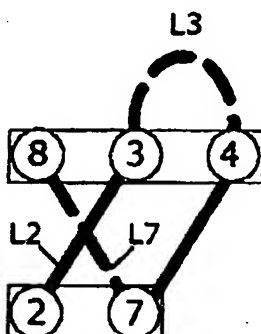
Fig. 2

## Structural Deviations

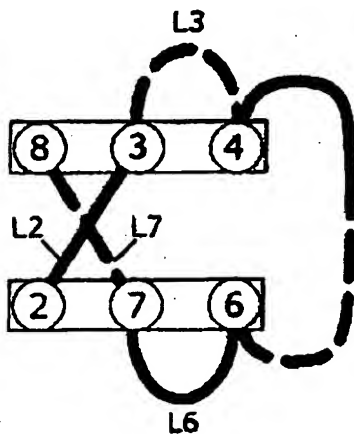
4 beta elements:



5 beta elements:

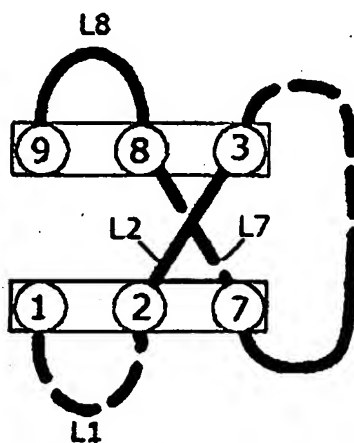


6 beta elements-a:



1GOY: Interleukin-1  
 receptor type 1

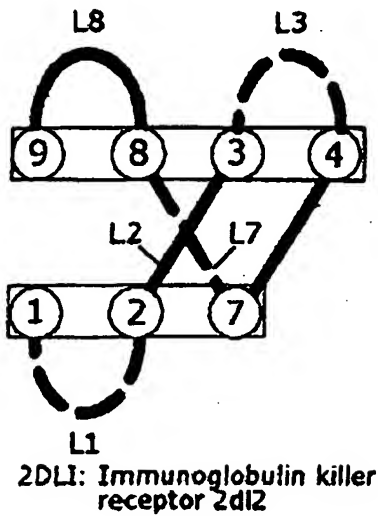
6 beta elements-b:



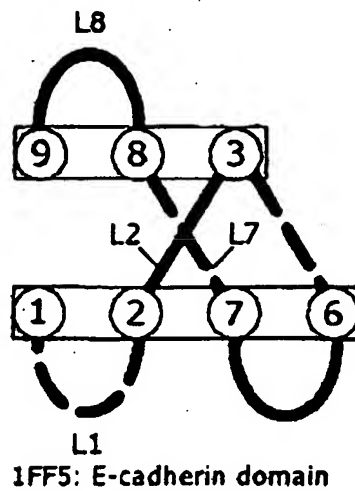
1188: Fc epsilon receptor  
 type alpha

Fig. 3a

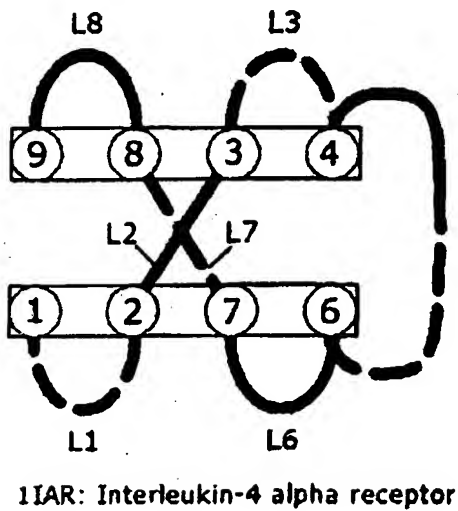
7 beta elements-a:



7 beta elements-b:



8 beta elements:



9 beta elements:

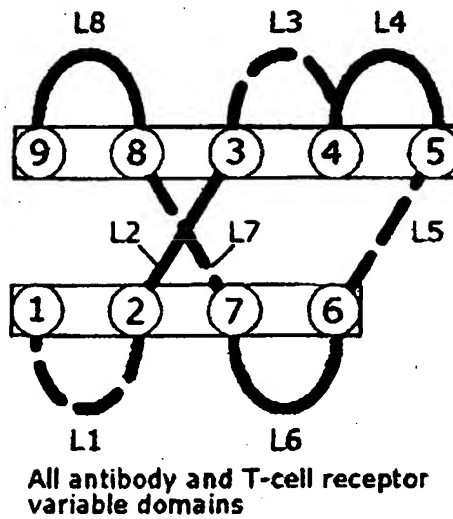


Fig. 3b

## Modular Affinity & Scaffold Transfer (MAST) Te

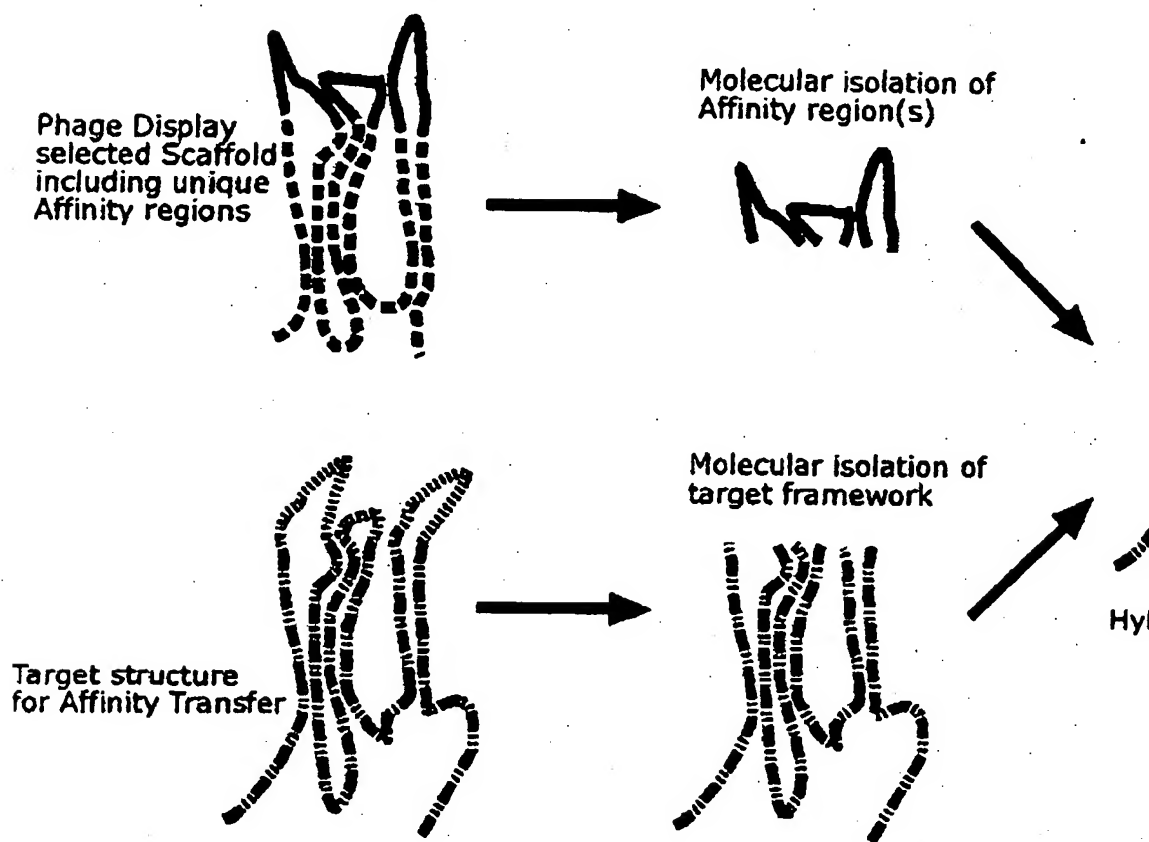


Fig. 4

# STRUCTURAL ALIGNMENT: EXAMPLES OF 1F2X V<sub>H</sub> CAMELID ANTIBODY VARIABLE FRAGMENT

	1	2	3	4	5	6	7	8	9
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1QD0	QVQLOE-SG--G-GLVQGGSLRLSCAASGYL	-----ASNGHGYGNGHFRQ-VPCK--EREFVAAIRWSG--KETMYKNDKSVKGRFTTISQDNKNTVYLQNMNSL-K-GEDTAVYYCAHRPVRVADIS---	-----LPVGFDTWGGGTQ-VTVS						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
8FAB	AVKLQV-AG--G-GVQDPEPSRLSCLASGFT	-----ISNYGCHHKVRO-APGK--GLEWVAIV--YNGSRTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTAVYYCARDPDIILT	-----AFSFDTWGGGTQ-VTVS						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1VSC	-PKIET-TPER-YLAQIGDSVSLTCTSTCE	-----SPFFSHRTQ-ID--	-----SPLNGKVTWCG--TSTLTMPV-S-PGNENSYLCTATCE						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1NS3	EQSLA-TC--V-----NVCVCTVYHG	-----AGSKTLIAGP-K--	-----GPIIIG--						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1F97	KGSVYT-AGS-D-VQVPPNESIKLTCTVSGHS	-----SPRVEKKEV-Q-GS--TIALVCYS	-----QITAPVADRVTFSS						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1ENF	VPPTD-LR--IETHGP--DTHRVTNAPPES	-----IDLTFNLFVRYSPVRNE--EDVAELSLIS	-----PSDNVVLTLNL-L-PGTEYVVSVSVEQNH						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
ICEB	PNAPKILG-L-CQAD--KAEIHWEOQGDN	-----RSPILHYTIQFN-TSFTPaSMDAAYEKV	-----PMTDSSEVVGMS						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1IAR	LEPGLNLT-VRIT-----NVAOTLLTNSNPFPDNYLYNHUTYAVNISE--NDPA--DEFIYHNTY	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1F2X	QVOLVE-SG--G-GSVQAGGSLRLSCAASGYL	-----VSTYCMGHFRQ-APGK--EREGVATIL	-----G--GSTYYGDSVKGRFTTISQDNKNTVYLQNMNSL-K-PEDTALYYCAGSTVASTGWCSTLRPYDYHYRGGGTQ-VTVS						
1F4H	EQFRL-SG--G--QTLEVTSEY-LFRHADNELLHAKVA-LDQ	-----PLASGEVP--LD--V--	-----APQGKQLIELPELPDQPE-saqQKLELTVRVVQPNATAK--seagNiSAWQ-OMR-LAEN						

## Figure elements explained:

Underlined domains represent (putative) beta-elements 1-9  
Capital letters indicate conserved structural amino acids  
- indicate the absence of amino acid residues

## Aligned protein domains from:

- 1F2X Single domain camelid antibody Cab-Ca05
- 1QD0 Camelid heavy chain variable domain
- 8FAB Heavy chain from human Iggl
- 1VSC Human Vcam-1
- 1NS3 Structure Of Hcv Protease (Bk Strain) from hepatitis C-virus
- 1F97 Soluble Part Of The Junction Adhesion Molecule From Mouse
- 1ENF Fragment Of Human Fibronectin Encompassing Type-III Repeats 7 Through 10
- 1CFB Drosophila neuroglian
- 1IAR Human Interleukin-4 receptor alpha chain complex
- 1F4H E. Coli (Lacz) Beta-Galactosidase (Orthorhombic)

Fig. 5

**Scaffold with V<sub>HH</sub> 1MEL CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A E G Y T I G P Y C M G W F R Q A  
ACGTGCCGTGCTGAAGGTTACACCATTGGCCCGTACTGCATGGGTGGTTCCGTCAGGCG  
P N D D S T N V A T I N M G G G I T Y Y  
CCGAACGACGACGACTACTAACGTGGCCACGATCAACATGGGTGGCGGTATTACGTACTAC  
G D S V K E R F D I R R D N A S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAACGCGTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A G D S  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGATTCT  
T I Y A S Y Y E C G H G L S T G G Y G Y  
ACCATTTACGCGAGCTATTATGAATGTGGTCATGGCTGAGTACCGCGGTACCGCTAC  
D S H Y R G Q G T D V T V S S  
GATAGCCACTACCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

**Scaffold with V<sub>HH</sub> 1BZQ CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A S G Y A Y T Y I Y M G W F R Q A  
ACGTGCCGTGCTAGCGGTTACGCCTACACGTATATCTACATGGGTTGGTTCCGTCAGGCG  
P N D D S T N V A T I D S G G G G T L Y  
CCGAACGACGACGACTACTAACGTGGCCACCATCGACTCGGGTGGCGGCGGTACCCTGTAC  
G D S V K E R F D I R R D K G S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAAGGCTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A A G G  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGCGGGTGGC  
Y E L R D R T Y G Q R G Q G T D V T V S  
TACGAAGTGGCGACCGCACCTACCGTCAGCGTGGTCAGGGTACCGACGTTACCGTCTCG  
S  
TCG

**Scaffold with V<sub>HH</sub> 1HCV CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A E G R T G S T Y D M G W F R Q A  
ACGTGCCGTGCTGAAGGTCGTACGGGTTGACCTACGATATGGGTTGGTTCCGTCAGGCG  
P N D D S T N V A T I N W D S A R T Y Y  
CCGAACGACGACGACTACTAACGTGGCCACGATCAACTGGGATAGCGCCCGTACGTACTAC  
G D S V K E R F D I R R D N A S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAATGCCTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A G G E  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGGTGAA  
G G T W D S R G Q G T D V T V S S  
GGCGGCACCTGGGATAGCCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

Underlined regions indicate specific affinity regions.

The sequence of underlined regions in each panel represent respectively loop L2 (~CDR1 and AR1), L4 (~CDR2 and AR2) and L8 (~CDR3 and AR4).

Fig. 6a

Stru utural t p logy of a primairy scaffold

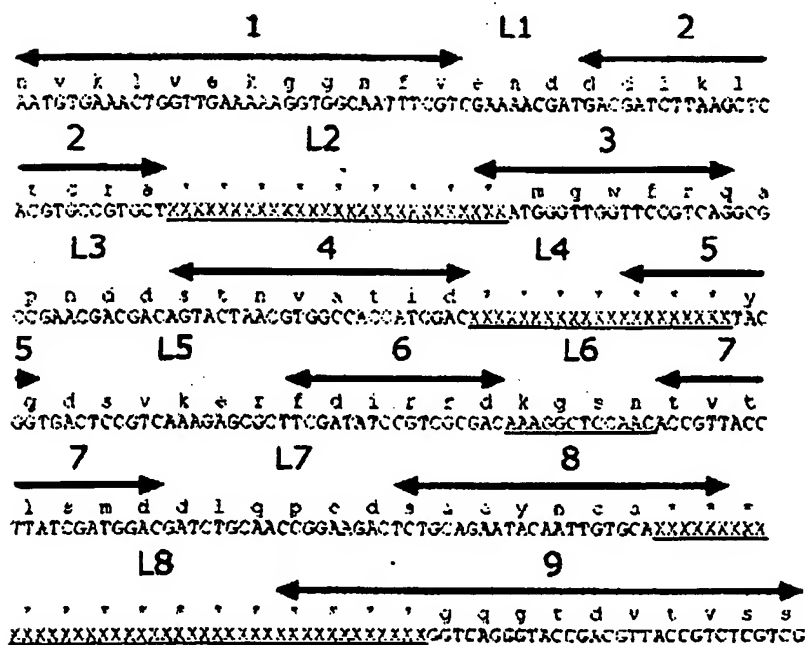


Fig. 6b